indicative of the molecule being useful in imaging and treating breast cancer.

a2 9. An antibody which specifically binds a Breast Cancer Specific Gene (BCSG).

a3 15. A method of treating breast cancer in a patient comprising administering to the patient a molecule which downregulates expression or activity of a Breast Cancer Specific Gene (BCSG).

16. A method of inducing an immune response against a target cell expressing a Breast Cancer Specific Gene (BCSG) comprising delivering to a human patient an immunogenically stimulatory amount of a BCSG protein so that an immune response is mounted against the target cell.

17. A vaccine for treating breast cancer comprising a Breast Cancer Specific Gene (BCSG).

REMARKS

Claims 1-17 are pending in the instant application. Claims 1, 2 and 8-17 have been withdrawn from consideration by the Examiner. Claims 3-7 have been rejected. Claims 1, 3, 4, 5, 6, 7, 8, 9, 15, 16 and 17 have been amended. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Restriction Requirement

The Examiner has made a Restriction Requirement as follows:

Group I, claims 1(a) and (c) (in part, as it reads on polynucleotides), drawn to a BCSG comprising a polynucleotide, classified in class 536, subclass 23.1;

Group II, claims 1(b) and 2, (in part as it reads on proteins), drawn to a BCSG comprising a protein classified in class 530, subclass 350;

Group III, claims 3-7, drawn to a method of diagnosing, staging and monitoring breast cancer, classified in class 435, subclass 4;

Group IV, claim 8, drawn to a method of identifying potential therapeutic agents, classified in class 435, subclass 7.1;

Group V, claims 9-10, drawn to an antibody, which binds to BCSG, classified in class 424, subclass 138.1;

Group VI, claims 11-12, drawn to a method of imaging breast cancer, classified in class 424, subclass 9.3;

Group VII, claims 13-15, drawn to a method of treating breast cancer, classified in class 424, subclass 183.1;

Group VIII, claim 16, drawn to a method of inducing an immune response, classified in class 424, subclass 184.1; and

Group IX, claim 17, drawn to a vaccine, classified in class 424, subclass 184.1.

The Examiner suggests that these Groups are distinct. Specifically, with respect to Groups I-II and V and III-IV and VI-VIII, the Examiner has acknowledged the Groups to be related. However, the Examiner suggests that the products of Groups I-II, and V may be used for a number of different unrelated processes. With respect to Groups I-II and V, the Examiner suggests that the claims are drawn to structurally and functionally different molecules. With respect to Groups III-IV and VI-VII, the Examiner suggests that the methods differ in steps, mode of operation, reagents needed and serve different endpoints and effects.

Applicants respectfully traverse this restriction requirement.

MPEP §803 provides two criteria which must be met for a restriction requirement to be proper. The first is that the inventions be independent or distinct. The second is that there would be a serious burden on the Examiner if the restriction is not required. A proper search of the prior art relating to BCSGs as used in the claims of Group III, should also reveal art relating to the diagnostic markers themselves, as set forth in Groups I and II, additional uses for the markers as set forth in Groups IV, VIII and IX, as well as antibodies against these markers and methods of

using these antibodies as set forth in Groups V, VI and VII. Thus, it does not appear that a serious burden would be placed upon the Examiner if restriction were not made.

Accordingly, since this Restriction Requirement does not meet both criteria as set forth in MPEP § 803 to be proper, it is respectfully requested that this Restriction Requirement be withdrawn.

However, in an earnest effort to be completely responsive, Applicants elect to prosecute Group III, claims 3-7, with traverse.

II. Objection to Specification

The Examiner has objected to the Abstract as not being in compliance with 37 C.F.R. 1.72(b). Accordingly, in an earnest effort to advance the prosecution of this case, Applicants are providing a replacement Abstract herewith which has been amended to enable the reader to ascertain quickly the character of the subject matter covered by this disclosure. No new matter has been added by this amendment.

The Examiner has also noted the use of the trademark TAQMAN in the specification and has requested that this be capitalized and accompanied by the generic terminology. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended the specification to capitalize TAQMAN and have provided

the generic terminology for this trademark where the term is first presented in the specification.

Withdrawal of these objections to the specification is respectfully requested in light of these amendments.

III. Rejection of Claims 3-7 under 35 U.S.C. § 112, second paragraph

Claims 3-7 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner suggests that recitation of "BCSG" without delineation of the full name of the entity, which the abbreviation denotes, is indefinite. Thus, in accordance with the Examiner's suggestion, Applicants have amended the claims at the first occurrence of the abbreviation in each claim to recite the full name "Breast Cancer Specific Gene". Withdrawal of this rejection is therefore respectfully requested.

IV. Rejection of Claims 3-7 under 35 U.S.C. § 112, first paragraph

Claims 3-7 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to

make and/or use the invention. The Examiner has listed several reasons as to why the instant disclosure fails to meet the enablement requirements including: the nature of the invention; the state of the prior art and predictability or lack thereof in the art; the amount of direction and guidance present; the presence or absence of working examples; the breadth of the claims; and the quantity of experimentation needed.

With respect to these reasons, the Examiner relies upon prior art references relating to BRCA1, BRCA2, p53 and BCSG1 to suggest that based on teachings in the art, in order for breast cancer to be diagnosed, it must be certain that changes in the expression levels of BCSG as compared to levels in normal breast are indeed indicative of breast cancer and not some other disease. Further, the Examiner suggests that the predictability of determining cancer or metastasis thereof in cells, tissue or bodily fluids that are not from the breast is uncertain because prior art relating to BRCA1, BRCA2, p53 and BCSG1 has only taught the diagnosis of cancer by determining the expression of BCSG in breast tissue alone.

The Examiner also suggests that given the teachings of unpredictability in the art relating to BRCA1, BRCA2, p53 and BCSG1, detailed teachings are required to be present in the disclosure in order for the skilled artisan to diagnose, stage and

monitor breast cancer as claimed. The Examiner suggests that such teachings are not present in the instant application.

Finally the Examiner suggests that one of ordinary skill in the art would be forced into undue experimentation to practice the invention as claimed because it would be extremely unpredictable to diagnose, monitor, and stage breast cancer or metastasis by determining the levels of BCSG in cells, tissues or bodily fluids unless these sample are from breast tissue and the levels clearly correlate with the presence of breast cancer. Applicants respectfully traverse this rejection.

At the outset, Applicants would like to clarify that the BCSGs of the present invention, described in the instant specification as comprising a polynucleotide of SEQ ID NO:1, 2, 3, 4, 5, 18 or 20 or a variant thereof, a protein expressed by a polynucleotide of SEQ ID NO:1, 2, 3, 4, 5, 18 or 20 or variant thereof which expresses the protein, or a polynucleotide which is capable of hybridizing under stringent conditions to the antisense sequence of SEQ ID NO: 1, 2, 3, 4, 5, 18 or 20, are different markers for breast cancer than BCSG1 as taught by Ji et al. and BRCA1, BRCA2 and p53. Accordingly, the Examiner's reliance on teachings relating to these different markers affecting the predictability or unpredictability of the instant invention is misplaced.

As set forth in MPEP § 2164.03, the predictability or lack thereof in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. Results evidencing the utility of the BCSGs of the present invention as diagnostic markers for breast cancer are presented in the specification beginning at page 20. The specificity of the BCSGs of the present invention as breast specific genes was first determined via CLASP, a data mining program which allows the identification of highly expressed organ and cancer specific genes. See pages 20 through 21 of the instant specification. Elevated mRNA expression levels were then detected in 4 of these markers in breast cancer samples using Real-Time quantitative PCR thus evidencing usage of CLASP as a tool for identifying cancer markers. Data evidencing a high level of tissue specificity as well as overexpression of BCSG-5 in breast cancer samples are set forth at pages 22 through 27. Data evidencing a high level of tissue specificity as well as overexpression of BCSG-1 in breast cancer samples are set forth at pages 27 through 32. Data evidencing a high level of tissue specificity as well as overexpression of BCSG-2 in breast cancer samples are set forth at pages 32 through 37. Data evidencing a high level of tissue specificity as well as overexpression of BCSG-3 in breast cancer

samples are set forth at pages 37 through 42. As shown by the review article provided herewith (Berns, A. Nature 2000 403:491-492), gene expression data such as provided in the instant application is used routinely by those of skill in the art to examine activity of a gene under various conditions. Accordingly, one of skill in the art could clearly routinely extrapolate results disclosed in the instant application of an increase in these BCSGs levels being indicative of breast cancer to the claimed invention. Further, those of skill in the art routinely extrapolate data relating to specificity of markers, such as provided for the markers of the present invention in breast tissue, to be indicative of metastasis and/or advanced stages of breast cancer when an increase in these markers is detected in cells, tissues or bodily fluids other than breast tissue. Thus, contrary to the Examiner's suggestion, the claimed invention is predictable when read in light of the teachings of the specification which clearly provide one skilled in the art with the ability to extrapolate the disclosed results to the claimed invention.

In an earnest effort to advance the prosecution of this case, and in accordance with data provided in the instant specification relating to an increase in BCSG levels being diagnostic for breast cancer, Applicants have amended step (b) of claim 3 to clarify that

an increase in determined levels of BCSG in said patient versus normal human control is associated with the presence of breast cancer.

Applicants also respectfully disagree with the Examiner's characterization of the prior art as teaching that in order for breast cancer to be diagnosed, it must be certain that changes in the expression levels of BCSG as compared to levels in normal breast are indeed indicative of breast cancer and not some other disease. Diagnosing is defined in Webster's Dictionary as the act or process of deciding the nature of a diseased condition by examination. Clearly, determining levels of a BCSG of the present invention in cells, tissues or bodily fluids in a patient as taught in the instant application constitutes an act or process of examination for deciding the nature of a diseased condition.

MPEP § 2164 sets forth the enablement requirement of 35 U.S.C. § 112, first paragraph. The enablement requirement refers to the requirement of 35 U.S.C. § 112, first paragraph that the specification describe how to make and how to use the invention. The invention that one skilled in the art must be enabled to make and use is defined by the claim(s) of the particular application. Contrary to the Examiner's suggestion that the instant specification lacks detailed teachings required to diagnose, stage

and monitor breast cancer, it is respectfully pointed out that the instant specification provides the sequence information for the BCSGs of the present invention as well as detailed methodologies for measuring BCSG levels in a patient. See pages 12-15. The specification also provides detailed methodologies for use of these markers to diagnose (see pages 8-10 of specification), stage (see page 10 of specification) and monitor (see page 10-11 of specification) breast cancer in patients. Further, as discussed in detail above, the instant specification also provides data understood by the skilled artisan to be demonstrative of the BCSGs of the present invention being diagnostic for breast cancer as claimed. Accordingly, the instant specification clearly teaches one of skill in the art how to make and use the invention as claimed.

It is therefore respectfully requested that the rejection of claims 3-7 under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Supplemental IDS

A supplemental IDS and requisite fee are provided herewith.

VI. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Respectfully submitted,

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Date: **December 17, 2001**

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Please amend the claims as follows:

1. (amended) A Breast Cancer Specific Gene (BCSG) comprising:

(a) a polynucleotide of SEQ ID NO:1, 2, 3, 4, 5, 18 or 20 or a variant thereof;

(b) a protein expressed by a polynucleotide of SEQ ID NO:1, 2, 3, 4, 5, 18 or 20 or a variant thereof; or

(c) a polynucleotide which is capable of hybridizing under stringent conditions to the antisense sequence of SEQ ID NO: 1, 2, 3, 4, 5, 18 or 20.

3. A method for diagnosing the presence of breast cancer in a patient comprising:

(a) determining levels of Breast Cancer Specific Gene(BCSG) in cells, tissues or bodily fluids in a patient; and

(b) comparing the determined levels of BCSG with levels of BCSG in cells, tissues or bodily fluids from a normal human control, wherein ~~a change~~ an increase in determined levels of BCSG in said patient versus normal human control is associated with the presence of breast cancer.

4. (amended) A method of diagnosing metastases of breast cancer in a patient comprising:

(a) identifying a patient having breast cancer that is not known to have metastasized;

(b) determining Breast Cancer Specific Gene (BCSG) levels in cells, tissues, or bodily fluid from said patient; and

(c) comparing the determined BCSG levels with levels of BCSG in cells, tissue, or bodily fluid of a normal human control, wherein an increase in determined BCSG levels in the patient versus the normal human control is associated with breast cancer which has metastasized.

5. (amended) A method of staging breast cancer in a patient having breast cancer comprising:

(a) identifying a patient having breast cancer;

(b) determining Breast Cancer Specific Gene (BCSG) levels in a sample of cells, tissue, or bodily fluid from said patient; and

(c) comparing determined BCSG levels with levels of BCSG in cells, tissues, or bodily fluid of a normal human control, wherein an increase in determined BCSG levels in said patient versus the normal human control is associated with breast cancer which is progressing and a decrease in the determined BCSG levels

is associated with breast cancer which is regressing or in remission.

6. (amended) A method of monitoring breast cancer in a patient for the onset of metastasis comprising:

(a) identifying a patient having breast cancer that is not known to have metastasized;

(b) periodically determining levels of Breast Cancer Specific Gene (BCSG) in samples of cells, tissues, or bodily fluid from said patient; and

(c) comparing the periodically determined BCSG levels with levels of BCSG in cells, tissues, or bodily fluid of a normal human control, wherein an increase in any one of the periodically determined BCSG levels in the patient versus the normal human control is associated with breast cancer which has metastasized.

7. (amended) A method of monitoring a change in stage of breast cancer in a patient comprising:

(a) identifying a patient having breast cancer;

(b) periodically determining levels of Breast Cancer Specific Genes (BCSG) in cells, tissues, or bodily fluid from said patient; and

(c) comparing the periodically determined BCSG levels with levels of BCSG in cells, tissues, or bodily fluid of a normal

human control, wherein an increase in any one of the periodically determined BCSG levels in the patient versus the normal human control is associated with breast cancer which is progressing in stage and a decrease is associated with breast cancer which is regressing in stage or in remission.

8. A method of identifying potential therapeutic agents for use in imaging and treating breast cancer comprising screening molecules for an ability to bind to Breast Cancer Specific Gene (BCSG) wherein the ability of a molecule to bind to BCSG is indicative of the molecule being useful in imaging and treating breast cancer.

9. An antibody which specifically binds a Breast Cancer Specific Gene (BCSG).

15. A method of treating breast cancer in a patient comprising administering to the patient a molecule which downregulates expression or activity of a Breast Cancer Specific Gene (BCSG).

16. A method of inducing an immune response against a target cell expressing a Breast Cancer Specific Gene (BCSG) comprising delivering to a human patient an immunogenically stimulatory amount of a BCSG protein so that an immune response is mounted against the target cell.

17. A vaccine for treating breast cancer comprising a Breast Cancer Specific Gene (BCSG).